Radiotherapy

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Introduction

With improvements in staging, surgery, and systemic therapies, the role of radiation treatment in children has changed dramatically over the past few decades. Improved cure rates as demonstrated in sequential clinical trials have shifted the focus from cure alone to cure with best long-term function and quality of life. This has particular implications for radiotherapy where the long-term consequences are well recognized. Over the same period pediatric radiotherapy has become more refined as a result of improvements in techniques for both planning and delivery of treatment. Whenever radiation therapy is being considered for a child the indications should be very carefully thought through and the role of radiotherapy in that child's management continually appraised.

Radiation can now be (almost) completely omitted from the treatment of some disease types, for example non-Hodgkin's lymphoma where it's only role is in palliation, relapsed or CNS disease.

What Is Radiotherapy

Radiotherapy (RT) is the treatment of disease (almost exclusively malignant tumors) with electromagnetic or particle radiation. This may be delivered as beams from outside the body (like an x-ray) often called XRT, or by using radioactive material, which is inserted (e.g., radioactive source), ingested (Iodine) or injected (mIBG). Most radiation treatment is external beam radiation and is delivered using a machine called a linear accelerator, which delivers photon radiation; some machines can also produce electrons. Rarely now cobalt sources are used, although historically they were very important. Some departments may have a proton beam treatment unit, although there is no suitable facility in the UK.

The energy from radiation is ionizing. This means that it disrupts the atomic structure of material it passes through, in this case human tissue. Ionization produces chemical and biological changes in tissues. These changes may be to any molecular cell component; however, the most important is damage to DNA, especially bonds between molecules.

This DNA damage may not be expressed biologically for years. Some cells will die quickly (apoptosis); however, others will do so at a later date when a damaged region of DNA is "used." Some cells function too poorly to divide but may die earlier than expected.

Normal tissue is affected in the same way as malignant tissue, but normal cells initially have more intact DNA and their DNA repair is better (especially in tissues with rapid turnover, for example, mucosa).

Radiobiology

Radiobiology is the study of the effects of radiation on tissues and how particular cells or tissue types are affected by the type of radiation, total dose given, dose per fraction, interval between fractions, and overall duration of treatment [4]. This has allowed the development of radiotherapy schedules; initially these were empirical but have now evolved with a strong scientific basis. Much of this data is from cell line work and may be expressed as SF2; this is the surviving fraction (of cells) after 2 Gy. Using this type of experimental data a comparison can be made between tumor types or treatment conditions.

Type of Radiation

The energy of a radiotherapy beam and what it is made up of (photons, electrons, or protons) will affect the way in which this energy is deposited in tissue and thus affect the tissue

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response to it. For example, low energy photons (orthovoltage or kilovoltage) are preferentially absorbed in bone and do not exhibit the skin-sparing phenomenon seen with megavoltage photon irradiation. For this reason orthovoltage radiotherapy can be particularly useful for treating skin or bone lesions. In children, however, it may cause greater disruption of bone growth in the longer term than higher energy treatment.

Total Dose

The total dose needed for different tumor types varies; some are more sensitive (e.g., lymphoma, leukemia), others are relatively resistant (e.g., osteosarcoma), many, however, are between these extremes. For example, we know that the dose needed to treat Ewing's sarcoma is greater than that needed for Wilms' tumor. This knowledge guides the recommended total dose delivered. The dose required doesn't vary with the age of the child – though the biology of a particular tumor may vary between a very young child compared with an older child (e.g., neuroblastoma). Radiation dose is commonly expressed as Gray (Gy) or centigray (cGy), where 100 cGy = 1 Gy.

Dose Per Fraction

If the total dose were delivered in a single treatment the antitumor effect would be excellent; however, the effect on normal supporting tissues would unfortunately be devastating. For the majority of situations where a large area or volume of the patient has to be treated this is unacceptable. There are two main exceptions to this, palliative treatment (where the total dose is lower), and small brain lesions. The latter can be treated with stereotactic radiosurgery (single treatment to a small area with a high dose using multiple fields) though this is not employed as often in children as in adults.

The total dose is therefore divided into a number of small doses or fractions, which are delivered on a daily (or more rarely twice a day) basis. This allows the normal tissues (and the tumor cells) a chance to repair some of the DNA damage. The reason radiotherapy works to kill tumor cells is that they do not repair DNA damage as efficiently as normal cells.

As the dose per fraction gets smaller, there is greater relative sparing of normal tissues, but a higher risk that tumor cells are also spared permanent damage.

This illustrates the reason why gaps or breaks in treatment are detrimental to clinical outcome; a break in treatment will allow time for more DNA repair. Clinical data bears this out, e.g., medulloblastoma, survival is linked to overall time of radiation treatment.

Interval Between Fractions

Traditionally a dose of radiotherapy is given daily with a 24 h interval between treatments. Shortening the interval between fractions, for example to 6–8 h, should result in a greater biological effect on both normal and tumor cells. If the interval is long enough for the normal tissue to recover, but not long enough for tumor tissue recovery, there will be a greater amount of damage to tumor cells. This type of radiotherapy delivery is called hyperfractionation. It poses logistic problems, as the working day is typically 8 h long. Treatment therefore has to be given first thing in the morning and last thing at night. It is difficult to deliver this type of treatment to an anesthetized child. As there are theoretical advantages in this approach it has been used in both Ewing's sarcoma and medulloblastoma, but does not yet represent a standard treatment approach.

Overall Time

Most radiotherapy departments' work only 5 days a week and some are unable to treat on bank holidays. These gaps in treatment are inevitable; however, it is important to make every attempt to avoid any other gaps in treatment, for example due to transport problems, the patient being too ill to receive treatment, or machine breakdown. When such gaps do occur an adjustment to the remaining treatment may need to be made, although this is not always possible. The result may be a poorer chance of disease control or a greater chance of long-term toxicity.

Typical Pediatric Treatment Schedules

Most children will be treated with fraction sizes of 1.8 Gy (range 1.5–2 Gy) per day, 5 days per week for 2–6 weeks, depending upon the indications for radiotherapy and the disease type.

Challenges of Pediatric Radiotherapy

When radiation treatment is delivered to a child there are a number of aspects that differ from an adult's treatment. These need to be taken into account by the radiotherapy team and department and may necessitate a change in practice compared with "normal" departmental policy [5].

Ensuring the cooperation and compliance of the child is vital if accurate high quality treatment is to be given. This is generally much easier in adult patients who can understand what they are being asked to do and follow instructions, even if they are uncomfortable or scared.

Most pediatric treatment regimens are complex and require different treatments to be dovetailed together. This may cause difficulties in booking radiotherapy as occasionally little warning can be given or dates need to be changed at short notice.

Children are particularly prone to long-term consequences of radiotherapy; growing tissues will ultimately display changes that will never be observed in a fully grown person. Many parts are immature and have to both develop and grow; both of these processes are liable to be affected by irradiation. A particular point of concern is the developing CNS, which is very sensitive to the detrimental effect of radiotherapy. Children under 3 years of age are at particular risk of neurocognitive changes; however, older children may also be affected.

These detrimental effects may be minimized by following the principles of radiotherapy to children, which encourage:

1. Using the lowest effective total dose
2. Using the smallest possible treatment volume
3. Using a low dose rate or dose per fraction
4. Treating over an appropriate overall time

Lowest Effective Total Dose

Dose response curves in radiotherapy are a sigmoid shape (see Fig. 10.1). A small decrease in dose may result in a big reduction in the antitumor effect. Th e risk of side effects can also be expressed with a curve of this shape. Although the total dose used has to be effective at dealing with the tumor, if it can be reduced a little this may significantly decrease the long-term toxicity.

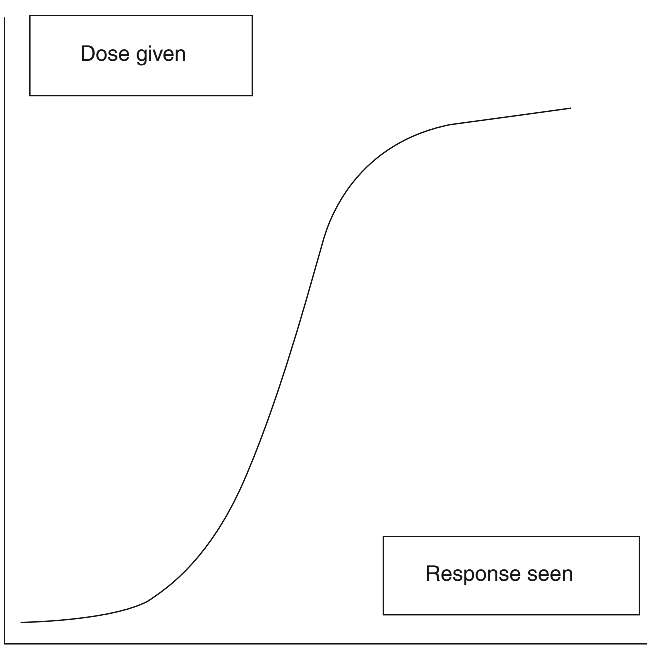

Fig. 10.1 Typical sigmoid dose-response curve

The small bowel, for example, presents a problem; toxicity is expressed rapidly and bowel is often unavoidably treated. Here, however, a small reduction in dose can result in a significant reduction in toxicity.

Smallest Possible Treatment Volume

Careful use of shielding and consideration of field arrangement will help to avoid structures at greatest risk of side effects. In this way the lens of the eye may be spared, or the jaw and developing teeth. The dose received by any area or organ at risk can be estimated during planning and in some cases measured during treatment.

Due to the known effects of radiotherapy on growing and developing tissues, symmetrical irradiation of the neck and spine is generally encouraged. For example, stage 1A Hodgkin's of the neck can be treated with radiotherapy alone, but conventionally the whole neck is irradiated even if the disease is unilateral.

In order to avoid an "organ at risk" (OAR), the beam arrangement or shape of the field may be manipulated, providing the target area is still treated appropriately. There may need to be a clinical decision about which toxicity is "preferable," or whether the target can be compromised. An example of this would be avoiding the femoral epiphyses at the expense of a higher rectal dose in a pelvic treatment.

Low Dose Rate or Dose Per Fraction

As previously discussed, small fraction sizes allow greater normal tissue repair, although if the dose per fraction is too low the desired effect on tumor cells will be reduced. Taken to its extreme, continuous irradiation at a low dose rate allows both recovery of normal tissues and tumor cell death. This is employed in low dose rate brachytherapy.

An Appropriate Overall Time

If treatment is extended over a prolonged time period (e.g., due to patient illness or machine breakdown) the antitumor effect is reduced.

Some protocols are looking at shortening the overall time a treatment is delivered over (e.g., hyperfractionated accelerated radiotherapy HART in medulloblastoma) to increase the antitumor effect.

Procedures

Decision to Irradiate

This is often made after discussion at a Multi Disciplinary Team (MDT) meeting where response on radiological, pathological, or clinical grounds is examined. Many therapeutic protocols specify that radiotherapy needs to be considered at a particular point in the child's overall management. In other cases radiotherapy may be one of the options when management strategy is being formulated [5].

No one takes this decision lightly. There are times when radiotherapy is technically easy but may not be in the child's best interests. On other occasions, radiotherapy may be the most appropriate choice but be technically very challenging.

Booking

All departments will have a system for arranging or booking radiotherapy planning and treatment. This will not only require patients demographic details (name, date of birth, address, etc.) but also the tumor type, site to be treated, need for anesthetic, and much more. A booking request can generally only be completed after a clinical oncologist (radiotherapist) has seen the patient. Departmental policy regarding prioritization varies. There is usually a classification into routine, urgent, and emergency treatments, based upon clinical need and tumor biology. Booking radiotherapy generally authorizes exposure to ionizing radiation (in the form of scans and x-rays), though formal written consent will be required for treatment.

Information Giving and Preparation

Before the child and parents or caregivers visit the department to begin the planning process they need to understand what will happen and what is expected of the child. Many departments will have information sheets or leaflets; some will have videos or websites. An initial visit to the department can be invaluable for children of all ages. This allows them to look around, see into the different areas and rooms they will need to enter, perhaps handle an immobilization device or to move the couch and obviously to ask questions.

Most departments will have an identified person who can act as a link for the family. This may be a radiographer, nurse, play specialist, or doctor.

It is increasingly recognized that pretreatment preparation is vital and may enable children who would otherwise need a general anesthetic (GA) to receive radiotherapy to manage without. Time spent at this stage can result in huge benefits later.

Anesthetic

There will always be some children who are not able to receive radiotherapy without sedation or GA. As children receiving treatment will be alone in the treatment room they need to be remotely supervised, completely still, and may need to wear a restraining/immobilization mask or device. General anesthetic with appropriate telemetry and support/recovery is usually preferred over sedation. For this to be a viable option all rooms used (mould room, simulator, treatment room with back-up room) must be fitted out appropriately. For instance, adequate lighting, anesthetic machine availability, available oxygen and suction, an induction and recovery area. Marks on the shell are used to accurately set up the treatment fields. Telemetry is in place and remotely viewed on a linked screen outside the room.

Venous access is desirable for anesthetic delivery and central venous access in the form of a tunneled line can be justified for daily anesthetics over a week or more. The alternative of using peripheral access will be preferred in some departments.

Pediatric anesthetists obviously play a central role in this part of the service. They must be adequately supported during the procedure and able to ensure the child recovers safely and appropriately each day. As many radiotherapy facilities are remote from a pediatric hospital there are obviously logistic difficulties that must be overcome.

Immobilization

Radiation treatment is planned with very little margin allowed for movement of the patient. It is known that if the patient stays "still" a margin of up to 10 mm needs to be added to the target volume depending upon the site treated. This can be challenging in adults but is more so in children, their smaller overall size means adding this extra margin will irradiate a proportionally larger amount of them.

In all patients, however, accurate and reproducible set up in a comfortable and stable position offers the best chance to get things right. A variety of aids are used here: knee bolsters, vacuum bags, body casts, foam wedges, and beam directing shells all have a place. Vacuum bags are plastic bags full of polystyrene beads that mould to the shape of the patient when the air is sucked out. They retain their shape over the course of treatment (a plug is put in) and can then be reused.

Plastic (or other rigid material) can be used to make a body cast in a similar way. These support part of body in the desired position and can be marked to aid set up.

Plastic beam directing shells (BDS) or masks are used for all head and neck treatments (Fig. 10.2). Here accuracy is more vital and small movements detrimental. Marks drawn on the shell mean that no marks need to be drawn on the patient.

Fig. 10.2 Anaesthetised child with immobilisation shell marks to guide radiotherapy delivery

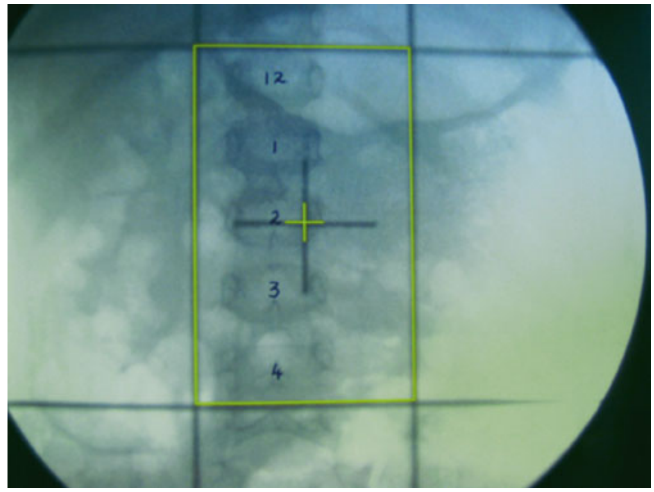

Fig. 10.3 Image showing treatment field edges and field centre. Demonstrates coverage of the full width of vertebral bodies

Planning

All planning and treatment is done with the child in the chosen position and immobilization device. All couch tops are identical in terms of geometry with respect to simulator and treatment beams. Simple planning can be done in a simulator using radiography to define the field to be treated, or by looking at the patient [1].

More complex plans require a CT scan first. Marks are drawn on the patient or radio-opaque markers stuck onto the skin. These will be used to make shifts in position (side to side or up and down) once the plan has been created. These all have to stay on until the patient comes for the next visit (often a week later).

CT scans are used to delineate the treatment volume on a computer-based system. The physics-planning department then creates a plan. This can be viewed on a computer system to look at dose distribution, hot spots, normal tissue doses, etc. before the patient attends for a treatment verification visit.

Verification is carried out before the patient starts treatment; often this is done using beams eye x-ray pictures, which can be checked against the physics plan. An example of this is seen in Fig. 10.3; this shows the field that will be treated for para-aortic nodal irradiation in Wilms' tumor; note the whole vertebral bodies are included to ensure uniform growth. Any changes to be made can be done at this stage. Permanent marks are needed to guide treatment set up on a daily basis. Tattoos are commonly used; these are pinprick marks made at one or more sites. While there is no difficulty performing a tattoo on an anesthetized or older compliant child, younger children may present a problem. Unfortunately, it is not possible to use topical local anesthetic as the precise position of the marks is critical and the location is not certain until the simulation visit is nearly completed. Play specialist input may be helpful for fearful children and many need some preparation.

Consent

Written informed consent prior to any radiation exposure is vital. It is required for all treatments, palliative and radical. The child will have been involved in discussions regarding treatment aims, side effects, and alternatives in an age-appropriate fashion. For those girls who could potentially become pregnant (over the age of 12 years in the UK) a signed declaration that they are not pregnant is required. No pregnancy test is undertaken unless there is uncertainty, in which case a spot urine test is performed.

Treatment

While the planning sessions may take 20–40 min, a treatment session is generally quicker. The total length of time a child is in the treatment room may be 10–30 min, depending upon their cooperation, how quickly the correct treatment position can be obtained, and the number of fields to be treated.

While the treatment beam is on, no one else is allowed in the treatment room. Unlike the simulator or CT simulator, the linear accelerator beam energy means that there is no window into the room. Patient observation is by closed circuit television (CCTV). There may be no physical door, just a long, curved corridor, so a shouted conversation is possible, or an intercom may be used.

Music or a story can be played on a CD player or the radio can be on. In some cases prior preparation is invaluable, for instance, asking the parents to practice with the child lying on a table at home, while listening to their chosen music with the parents waiting outside the door. The child can judge how far into the music or story they need to lie for.

It does not hurt to receive radiotherapy. Most patients are not aware of anything during exposure. Side effects may occur hours or days later.

Palliative Treatment

Palliative radiotherapy needs to be quick, simple, and effective. There is much less need to be concerned about the long-term side effects, providing short-term toxicity can be minimized and remain acceptable. Palliative treatments may be given in a single dose or a daily dose over a shorter period of time (a week for example). It is generally possible to get palliative treatment started within a few days of making the decision to irradiate.

In some cases where cure is unlikely aggressive palliative radiotherapy is called for, in the same way that intensive chemotherapy regimens may be used in this situation. For instance, irradiating as many of the disease sites as possible after completion of chemotherapy is suggested for metastatic Ewing's sarcoma, even though this may call for several areas to be treated. Decisions about how this type of recommendation is interpreted need to be made carefully.

Surgical Procedures to Reduce Toxicity of Radiotherapy

In some cases it is possible to insert a sling or mesh to lift small bowel away from the area to be irradiated; tissue expanders can be used in a similar way to push small bowel or other organs away from the irradiated area. Figure 10.4 shows a patient with a tissue expander in his pelvis. The red line shows the target volume and the treatment beams are indicated. The tissue expander helped to keep small bowel out of the treated area. Tissue expanders can be removed after treatment has been completed; a mesh may be absorbable. This approach is only valuable if it is possible to move structures such as the bowel away from the area to be treated. Early and comprehensive discussions between the surgeon, radiotherapist, and radiologist are needed if this is being considered.

Gonads can occasionally be moved to a safer area. If this is being considered it is important to discuss the proposed new location with the radiation therapist prior to surgery. It may be helpful to mark their new position with a clip for localization purposes on the planning images. In this way a dose estimate can be calculated prior to irradiation.

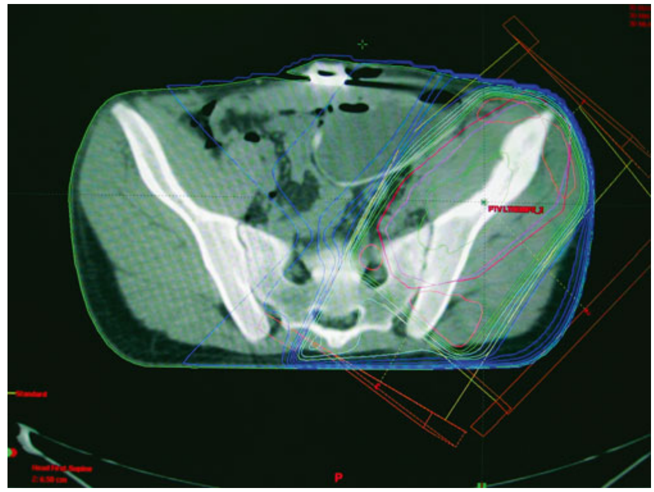

Fig. 10.4 Pelvic CT scan showing spacer, target volume, beam arrangement and isodoses

If any clips are placed at the time of surgery these will be seen at radiotherapy planning. If the operation record states where these are in relation to the tumor bed or at-risk area it can allow the radiation target to be placed with greater certainly. If, however, the clips were placed for hemostasis this should be annotated, as they would not need to be included in the target. Titanium clips are preferred.

Patients with a cystic component to a brain tumor will benefit from aspiration of the cyst to reduce its volume, even if debulking of the tumor is not feasible. The benefit may be seen in terms of clinical improvement; however, from a radiation treatment point of view a large cyst will require larger radiation treatment fields than a small cyst. Care must be taken in this situation to monitor the cyst for reaccumulation as this might push the edge of the cyst or tumor outside the volume being treated.

Surgeons have a common role in placing tunneled central lines or ports and occasionally enterostomy tubes. When required these allow the treatment to be given with a minimum of delay or upset to the child.

Timing of Radiotherapy with Respect to Surgery

Many pediatric oncology treatment protocols specify the sequencing of different treatment modalities, in particular if surgery should precede radiotherapy. There are some situations where preoperative radiotherapy can be considered and may have advantages. This predominantly occurs in the management of those soft tissue sarcomas where both radiotherapy and surgery are required. In adult sarcoma practice there does not appear to be any difference in survival for patients treated with preoperative compared with postoperative radiation for limb tumors. There is, however, a greater risk of serious postoperative wound complications in the group treated with preoperative radiotherapy. This result may not be directly applicable to pediatric practice as postoperative wound complications are much less common than in adults.

Adverse Effects and Management

Side effects are well recognized and depend a great deal on the area being treated. They are usually divided into acute effects (those seen during the period of irradiation or shortly after) and late effects (these may take months or years to become apparent) [5].

Acute Effects

These are not significantly worse in children than in adults – though they may cause greater distress and require careful management.

Most of these only affect the regions through which the irradiation passes. General side effects, however, occur, such as lethargy or tiredness regardless of the region treated. These are seldom severe in children and many experience no change in their activity levels. Nausea and vomiting may occur if the bowel, stomach, or liver are treated and can also be a problem with some CNS treatments. A standard antiemetic approach with an HT3 antagonist such as ondansetron or granisetron without steroids is usually sufficient. In some cases anorexia due to treatment may necessitate enteral feeding (e.g. craniospinal irradiation).

Skin and mucosal reactions develop during the course of treatment and generally settle rapidly without sequelae, the exception being some severe reactions, which may heal with scarring. It is rare for skin reactions to become severe in children; the doses used are lower than for many adult treatments and recovery more rapid. There are of course exceptions to this, which are usually predictable and dose related. The mucosa affected includes the lining of GI tract, GU tract, and respiratory system. Mucositis may be severe, particularly in those children who are receiving concomitant chemotherapy; occasionally parenteral opiate analgesia and feeding are needed.

Hair loss when a hair bearing area is irradiated develops after 10–14 days. Many children will already have alopecia due to chemotherapy. In rare cases radiotherapy causes permanent hair loss or thinning; this depends upon the total dose, comorbid factors, concomitant chemo, and dose received by hair follicles. Some treatments predictably cause a recognizable pattern of permanent thinning (e.g. posterior fossa boost for medulloblastoma treatment).

Those patients who have received prior or concomitant chemotherapy with drugs that may exacerbate the side effects of radiotherapy should be monitored with extra vigilance. They may develop radiation reactions of greater severity than expected.

Very few patients have a genetic radiation hypersensitivity syndrome (e.g., Ataxia Telangiectasia). Radiation should be avoided in these patients as acute side effects can be devastating or life threatening.

Late Effects

These occur after a time lag of several years or decades. DNA damage during radiotherapy may not be manifested until many years later. Many long-term side effects are a result of damage to endothelial cells lining small blood vessels. This leads to proliferation of small vessels, fibrosis, necrosis, or end organ failure.

The range of problems a child might be at risk of can be predicted from the treatment plan. However, while some of the problems are inevitable, their extent or severity may vary (for example, organ function, growth, or neurocognitive impairment). Other problems are not inevitable, but potentially very serious if they occur (for example, second malignancy).

Impairment to organ function after irradiation depends upon the type of organ involved. In some cases a small part of the organ (e.g., liver or kidney) can be irradiated to a high dose providing enough is left untreated. This is particularly important in those patients with only one kidney after a nephrectomy for Wilms' tumor or neuroblastoma. In other cases (such as spinal cord) no part of the structure can receive a high dose without significant risk of serious sequelae. Figure 10.5 shows a CT planning scan of a child with neuroblastoma; both kidneys are functioning and preserved after surgery. Unfortunately, the tumor bed and resected nodal area need to be irradiated. The red outline shows the tumor bed; the nodal area is not seen on this view as it is situated more anteriorly. The yellow rectangle shows the treatment field that has been further shaped by a multileaf collimator (MLC) indicated by the orange line. In this case treating part of both kidneys is unavoidable, but manageable as the total dose needed is low and enough of each kidney is left unirradiated.

Doses of 25–30 Gy result in failure of soft tissue development (rather than true atrophy). Thirty Gy will inhibit future bone growth, although within a bone there will be cells

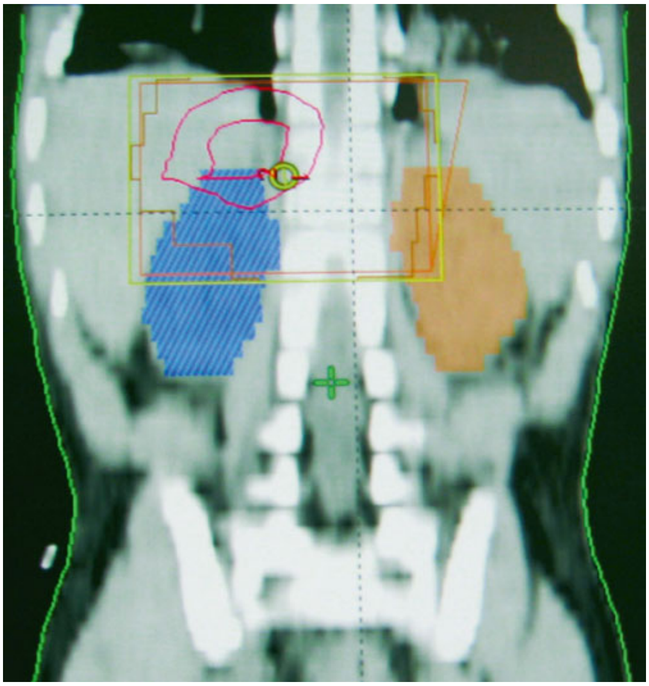

Fig. 10.5 Saggital reformatted planning CT scan showing position of kidneys, target area (*red*) and edges of the anterior treatment field (*yellow*)

already committed to "growing" which may produce a further 1–1.5 cm of postirradiation bone lengthening. Less than 30 Gy to bone will also affect growth, but not so severely and as little as 10 Gy can still impair bone and soft tissue growth; this may result in visible cosmetic asymmetry, absence of breast development, scoliosis, or functional problems (e.g. length discrepancy).

As the developing CNS is very sensitive to irradiation, particularly in younger children, developmental delay and neuropsychological impairment are a significant concern. Irradiation is avoided wherever possible. When it is required to effect a cure, careful monitoring and appropriate counseling and advice are imperative.

Second tumors are a devastating consequence of therapy. When they occur, there is generally a lag time of several years and they occur in the region exposed to irradiation [7]. These patients may be susceptible to developing more than one malignancy for a number of additional reasons: genetic factors, use of alkylating and other agents in chemotherapy, and if cured the prospect of a long life ahead.

Figure 10.6 illustrates the fields required for whole lung and renal bed irradiation in a patient with Wilms' tumor and pulmonary metastases. It can be seen from these treatment fields that the large treated area leads to the possibility of serious late effects – especially if the child is very young at the time of treatment. In a girl, both breast buds will be included in these fields; this may result in breast hypoplasia or poor development during puberty and in some cases requires breast augmentation in later life.

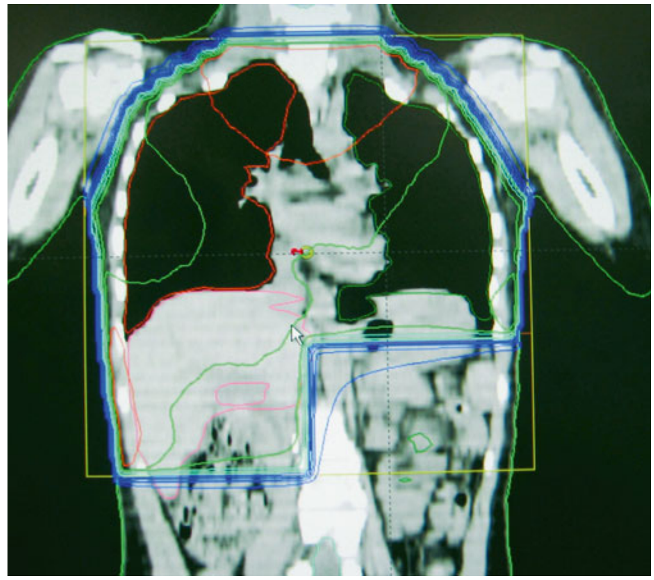

Fig. 10.6 Saggital reformatted planning CT scan showing fields for a patient with Wilms tumour requiring radiotherapy to both lungs and right flank

Other Techniques

Brachytherapy

This term encompasses treatment that is given by a source emitting radiation; this is inserted into the body or less frequently placed on the outside [2, 6]. These sources are made into a solid object such as wire (iridium), seed (gold), or a flat plaque (ruthenium).

There are a number of different ways this type of treatment can be administered; insertion or application under anesthesia is generally required. Whenever an active source is used, full radiation protection procedures are employed.

The advantage of this approach is that a high dose can be delivered to a small, defined volume. This is particularly advantageous in children, as surrounding organs at risk will receive a lower dose than with conventional external beam radiotherapy. However, there are a number of problems and brachytherapy is not suitable in many situations requiring radiotherapy. The major difficulties are compliance (treatment may require several days in a protected room, with limited close family contact and uncomfortable tubes or sutures), clinical experience, low level of supporting published evidence and concern about long-term effects (these will still occur). Close collaboration between all involved specialties is obviously required, as is specialist accommodation and experience in dealing with this type of treatment. As a result there are only a few very specialized centers where this treatment is offered.

Stereotactic Radiosurgery (SRS)

This refers to the very accurate delivery of a single high dose of radiotherapy using multiple thin beams [2]. At present it is only possible to do this if the area to be treated is in a site which can be immobilized very precisely in order that the target can be accurately localized (eg within brain). It also needs to be small enough (a few centimeters), and not too close to a critical structure (brainstem or optic nerves, for example). This type of treatment causes radionecrosis and there are biological uncertainties about the effect of such a treatment on adjacent normal structures. There are a limited number of suitable situations in pediatric practice, but some small brain lesions may be suitable.

Stereotactic Radiotherapy

This is similar to the SRS (above), however rather than a single treatment on 1 day, multiple treatments are given over a number of weeks. The criteria are similar to SRS except it is employed for potentially curable situations.

Proton Beam Irradiation

Protons are another type of energy (charged particles) that can be artificially produced (by a cyclotron) and used therapeutically [2]. They are available in a few centers and have very different physical characteristics to photons. Their principle advantage is that the energy deposition within tissue falls off abruptly at a defined depth within tissue. This may greatly reduce the volume of tissue exposed to the damage caused by radiation and hence the acute and long-term side effects. Not all situations requiring radiotherapy would be suitable for proton beam irradiation, and in some cases it would offer limited advantages over conventional therapy. However, there are an increasing number of situations where its advantages are being recognized as a way of reducing exposure of normal tissue or increasing dose to a focused target area. Whilst proton beam facilities are available in many countries, there are currently none in the UK for any treatment except intra ocular disease (uveal melanoma).

Proton therapy is currently funded by the UK for certain indications. These patients are treated in the USA or mainland Europe.

Intensity Modulated Radiotherapy (IMRT)

This term refers to a way of delivering conventionally fractionated radiotherapy that may have significant advantages over treatments using fixed beam shaping [2]. It aims to create a uniform dose distribution in the target area by delivering a nonuniform dose to the treatment fields. It requires the shape of the treatment field to constantly change during a treatment and typically the number of treatment fields is greater than the usual 2–4. The advantage in shaping the high dose treatment region around the target while sparing adjacent normal structures may allow the dose to tumor to be increased; this is particularly important in those situations where the tumor is relatively resistant. Equally important is the ability to spare a critical structure that is sensitive to radiation (for example, the spinal cord). There is, however, concern about the great integral dose of radiation received by the whole body from this type of approach which may ultimately be expressed as a higher number of patients developing second tumors in the decades to come [3].

There are many variations of IMRT. These depend upon both the hardware (treatment machine) and software (planning systems) that a particular center is using.

Examples include: VMAT = Volumetric Modulated Arc Therapy
Tomotherapy = Helical IMRT
IGRT = Image guided Radiotherapy, of which Rapid Arc is one example
IMPT = Intensity Modulated Proton Therapy

These are in constant development with new acronyms appearing frequently. The advantages or disadvantages of one over another may be relatively small. Longer follow up is needed to examine outcomes.

Whilst IMRT is increasingly available it is still not routine practice everywhere, and in some situations will not offer advantages over conventional treatment. Its place in pediatric radiotherapy is increasing but continues to be evaluated.

Therapeutic Radioisotopes

This refers to the administration of a radiolabeled target molecule that is specific to certain cells. These cells will be irradiated and therefore damaged. These compounds may be injected or ingested, and may be given alone or in combination with conventional chemotherapy.

The commonest of these is mIBG therapy for neuroblastoma. This is a useful palliative treatment and currently under investigation as part of a curative approach for advanced disease. It requires appropriate care and isolation of the child after treatment to comply with radiation protection legislation. Typically a child needs to be isolated with limited close contact for several days. Thyroid blockade with iodine is needed. It is, however, a tolerable and often very effective treatment.

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